REMARKS

Claims 1, 2, 4, 8 and 12 are amended.

Support for the amendments made to claim 1 is found in the Specification at, for example, Page 1, lines 1-2; Page 7, lines 1-14; Page 8, lines 10-11; and Page 13, lines 24-27.

Support for the amendments made to claim 2 is found in the Specification at, for example, Page 13, lines 3-5.

Claim 4 is amended to depend from claim 1 and to provide further clarity.

Support for the amendments made to claim 8 is found in the Specification at, for example, Page 9, lines 17-18.

Support for the amendment made to claim 12 is found in the Specification at, for example, Page 12, the last line to Page 13, line 2.

Claim 14 is amended to depend from claim 1.

Claims 3, 13, 16, 18, and 20 are canceled without prejudice.

New claims 21-41 are presented.

New claim 21 obtains support from the Specification at, for example, at Page 3, lines 2-4; and Page 13, line 28 to Page 14, line 8.

New claim 22 is supported by the Specification at Page 2, lines 21-29; and Page 16, second to last line to Page 17, line 8; and original claims 1 and 11. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l).

New claim 23 obtains support from the Specification at, for example, Page 3, lines 2-4; and Page 13, line 28 to Page 14, line 8.

New claim 24 obtains support from the Specification at, for example, Page 8, lines 12-13; and original claim 4. (Id.)

New claim 25 obtains support from the Specification at, for example, Page 16, lines 19-20; and original claim 5. (Id.)

New claim 26 obtains support from the Specification at, for example, Page 8, lines 19-21; and original claim 8. (Id.)

New claim 27 obtains support from the Specification at, for example, Page 9, lines 1-4; and original claim 10. (Id.)

New claim 28 obtains support from the Specification at, for example, Page 13, lines 3-5; and original claim 2. (Id.)

New claim 29 obtains support from the Specification at, for example, Page 16, second to last line to Page 17, line 8; and original claim 11. (Id.)

New claim 30 obtains support from the Specification at, for example, Page 17, lines 18-30; and original claim 12. (Id.)

New claim 31 obtains support from the Specification at, for example, Page 2, lines 21-29; and Page 17, lines 18-30; and original claims 1 and 12. (Id.)

New claim 32 obtains support from the Specification at, for example, Page 2, lines 21-29; and Page 7, lines 1-14; and original claim 1. (Id.)

New claims 33-40 each obtain support from the Specification. See, for example, the respective support cited above for claims 23-30.

New claim 41 obtains support from the Specification at, for example, Page 15, second to last line to Page 16, line 11; and Page 16, lines 22-26.

No new matter has been added.

Obviousness Rejection

Claims 1-10 and 13-20 were rejected under 35 U.S.C. § 103(a) as obvious over Dale, U.S. Patent No. 2,797,215 ("Dale '215"). (Paper No. 20080414 at 2.)

Dale '215 discloses the production of riboflavin crystals of type A, i.e. anhydrate I, from either type B, i.e., a mixture of anhydrate II and monohydrate, or type C, i.e., tetrahydrate. (Col. 2, lines 36-40.) For generation of type B and C crystals, Dale '215 discloses that synthetically produced riboflavin crystals are dissolved in an aqueous alkaline solution, filtered and acidified, followed by precipitation of type B and/or C crystals. Dale '215 discloses that these crystals are further transformed via boiling into type A crystals. (See, e.g., Col. 2, lines 48-60.)

In making the rejection, the Examiner asserted that "Dale teaches the purification of riboflavin which steps includes [sic] the preparation of a first crystalline form that is converted into a second form of crystalline form at 95-98 deg C which is further dried which is presumed to be essentially anhydrous crystals. In addition, the process as disclosed indicates that seeding yields better results for the conversion see column 4, first full paragraph." (Id.)

The Examiner acknowledged that "[t]he reference does not disclose conditions whereby the transforming step contains undisclosed conditions, not present in the instant claims that decompose 'diluted DNA'". (Id.)

The Examiner asserted, however, that "[i]t is presumed that the process conditions of the reference contain the requirement of decomposing diluted DNA absent a showing to the contrary." (Id.)

In addition, the Examiner asserted that "[t]he reference teaches the purification of riboflavin from one crystalline form A B or C [sic] to a different crystalline form which includes conditions of employing seeding with a riboflavin crystalline form as well as temperature requirements as disclosed in the specification." (Id. at 3.)

To further prosecution, claim 1 has been amended to recite a "[p]rocess for the purification of fermentatively produced riboflavin that has at least one impurity which is a DNA comprising the steps of:

(a) precipitating a first crystalline form of fermentatively produced riboflavin,

(b) isolating the first crystalline form of riboflavin,

(c) transforming the first crystalline form of riboflavin into a second crystalline form of riboflavin under conditions that decompose diluted DNA, and

(d) isolating the second crystalline form of riboflavin,

wherein the first crystalline form of riboflavin is a riboflavin hydrate."

New claim 32 has been added which recites "[a] process for decreasing the DNA content of riboflavin crystals comprising the steps of:

(a) fermentatively producing riboflavin in a fermentation broth,

(b) precipitating and isolating riboflavin crystals of a first crystalline form of riboflavin from the fermentation broth,

(c) transforming the crystals of step (b) into a second crystalline form of riboflavin which is a thermodynamically more stable form of riboflavin than the first crystalline form, and

(d) isolating the crystals of step (c)."

Also, new claim 41 is presented which recites "[a] process for removal of DNA from fermentatively produced riboflavin crystals comprising transforming a first crystalline form of riboflavin obtained from the fermentatively produced crystals into a second crystalline form of riboflavin."

It is also noted that the subject matter of prior claims 11 and 12 which the Examiner deemed allowable if rewritten to incorporate the base claim(s), has been added as new claims 22 and 31.

It is well settled the Examiner bears the burden to set forth a *prima facie* case of unpatentability. *In re Glaug*, 62 USPQ2d 1151, 1152 (Fed. Cir. 2002); *In re Oetiker*, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); and *In re Piasecki*, 223 USPQ 785, 788 (Fed. Cir. 1984). If the PTO fails to meet its burden, then the applicant is entitled to a patent. *In re Glaug*, 62 USPQ2d at 1152.

When patentability turns on the question of obviousness, as here, the search for and analysis of the prior art by the PTO should include evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and modify the document(s) relied on by the Examiner as evidence of obviousness. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1731-32 (2007) (the obviousness "***analysis should be made explicit***" and the teaching-suggestion-motivation test is "***a helpful insight***" for determining obviousness) (emphasis added); *McGinley v. Franklin Sports*, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). Moreover, the factual inquiry whether to modify document(s) must be thorough and searching. And, as is well settled, the teaching, motivation, or suggestion test "***must be based on objective evidence <u>of record</u>***." *In re Lee*, 61 USPQ2d 1430, 1433 (Fed. Cir. 2002) (emphasis added). *See also*

Examination Guidelines for Determining Obviousness, 72 Fed. Reg. 57526, 57528 (October 10, 2007) ("The key to supporting any rejection under 35 USC § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious.").

Respectfully, we submit that the rejection is devoid of a proper § 103 analysis in support of the proposed modification. All that is there are conclusory statements such as the assertion that "[i]t is presumed that the process conditions of the reference contain the requirement of decomposing diluted DNA absent a showing to the contrary." (Paper No. 20080414 at 2.) And, although the Examiner has made various statements regarding Dale '215, the Examiner has not included a statement as what the Examiner regards as obvious.

Here, what the rejection should have done, but did not, was to explain on the record ***why*** one skilled in this art would modify the disclosure of Dale '215 in the manner proposed by the Examiner to arrive at the claimed process for the purification of riboflavin. As is well settled, an Examiner cannot establish obviousness by locating one or more documents which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done. *Takeda Chem. Indus., Ltd v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. June 28, 2007) (citing *KSR*) (indicating that "it remains necessary to identify ***some reason*** that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound") (emphasis added); *Ex parte Levengood*, 28 USPQ2d 1300, 1301-02 (BPAI 1993). But this is precisely what the Examiner has done

here. Thus, the rejection is legally deficient and should be withdrawn for this reason alone.

Dale '215 does not disclose the purification of fermentatively produced riboflavin. Dale '215 does not even recognize the problem of riboflavin crystals obtained by fermentative production which have at least one impurity such as DNA adsorbed at the surface of the riboflavin crystals and/or included in the crystal grid (occlusion), both of which inhibit the decomposition of DNA. (Specification, e.g., Page 13, lines 24-27; Page 7-9.) No suggestion or motivation to achieve the presently claimed processes is found in Dale '215.

Dale '215 provides no suggestion or motivation to provide a process for the purification of riboflavin in accordance with the claimed invention of providing a first crystalline form of riboflavin which is then transformed into a second crystalline form of riboflavin. By providing a first crystalline form, the Specification discloses that the transforming step allows for "the full disruption of the crystal grid which is immediately followed by a re-crystallization of the riboflavin molecules in the form of [the second crystalline form]." (Page 16, lines 23-25.) The Specification further discloses that during this step "[i]mpurities, in particular DNA, are liberated and fully released and diluted into the surrounding medium." (Page 16, lines 25-26.)

Also, Dale '215 provides no suggestion to perform such a crystalline transformation wherein the first crystalline form is thermodynamically less stable than the second crystalline form of riboflavin, as presently claimed. Moreover, Dale '215 fails to suggest performing such a crystalline transformation under conditions that decompose diluted DNA. As stated in the Specification, the "DNA associated with the

riboflavin crystals can be decomposed rapidly when the crystal grid breaks up by the transformation of the first crystalline form of riboflavin under the conditions of the purification." (Page 16, lines 2-4.) In the Dale '215 process, on the other hand, no first crystalline form or intermediate in the preparation of Type A crystals is produced.

Dale '215 further does not suggest preparing a first crystalline form which is riboflavin hydrate, as claimed. Moreover, Dale '215 makes no disclosure of riboflavin hydrate at all. As disclosed in the present Specification, the "form of riboflavin which spontaneously precipitates from the fermentation broth is not necessarily the desired first crystalline form of riboflavin." Page 8, lines 14-16. One skilled in the art would not be led to try to produce a riboflavin hydrate as a first crystalline form (which is not the final desired crystalline product) in view of the lack of any hint or direction from Dale '215 to do so or even how to do so.

Also, the addition of seed crystals as presently claimed is not disclosed or suggested by Dale '215. Dale '215 discloses adding seed crystals to a solution of boiled riboflavin crystals. (Col. 4, lines 8-11.) Dale '215 thus uses seed crystals to accelerate obtaining Type A crystals from the starting material crystal of crude or impure Type A, B or C crystals. The seed crystals of the present claims, on the other hand, are added to the fermentatively produced riboflavin to induce the precipitation of the first crystalline form. The present claims provide in addition to the precipitation of the first crystalline form, a transformation step to the second crystalline form. As indicated, the claimed process permits the purification of fermentatively produced riboflavin with reduction of DNA content associated with riboflavin obtained from fermentative

production. Dale '215's use of seed crystals in no manner renders the present claims obvious.

In view of the foregoing, the rejection has been rendered moot. Reconsideration and withdrawal of the rejection are respectfully requested.

Objection to Claims 11 and 12

Claims 11 and 12 were objected to as being dependent upon a rejected base claim. (Paper No. 20080414 at 3.)

The Examiner acknowledged, however, that claims 11 and 12 "would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims." (Id.) In this regard, the Examiner asserted, "The reference does not disclose the process steps of heating in the range of 60 deg C and 75 deg C since the specific range in the reference is 95-98 deg C. The reference also does not teach or disclosure process step of claim 12." (Id.)

Present claims 11 and 12 depend from an amended claim 1. (Claim 12 is also amended.) As indicated above, it is submitted that amended claim 1 is allowable. Withdrawal of the objection as to current claims 11 and 12, therefore, is requested.

As suggested by the Examiner, former claims 11 and 12 have been rewritten as new claims, each incorporating the subject matter of the former base claim, claim 1. These are presented as new claims 22 and 31 which are adapted from former claims 11 and 12, respectively. The Examiner has indicated that claims presenting subject matter as embodied by presently submitted claims 22 and 31 would be allowable.

It is respectfully submitted that the objection has been rendered moot. Removal of the objection is requested.

For the reasons set forth above, entry of the claim amendments, withdrawal of the rejections and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on October 20, 2008.

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Respectfully submitted,

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